PATENT COOPERATION TREATY

TRANSLATION

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	26.10.2004
Applicant's or agent's file reference: 04-058-PCTJP	FOR FURTHER ACTION: See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2004/012238	19.08.2004	22.08.2003

International Patent Classification (IPC) or both national classification and IPC
C12N15/09, C07K14/47, C12N5/08, A61K35/26, A61P35/00, A61P37/04

Applicant
TAKARA BIO INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/JP	Authorized officer
Facsimile No.	Telephone No.

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Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☒ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☒ in computer readable form

c. time of filing/furnishing

☐ contained in the international application as filed.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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Box No. IV Lack of unity of invention

1. ☐ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has:
   - ☐ paid additional fees
   - ☐ paid additional fees under protest
   - ☐ not paid additional fees

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is
   - ☐ complied with
   - ☒ not complied with for the following reasons:

As disclosed in document 1 listed below, a technique for inducing cytotoxic T lymphocytes using fibronectin and a fragment thereof (e.g. a VLA-4 binding domain, VLA-5 binding domain, or heparin binding domain) was known in the art before the time of filing of the present application; therefore, said technique cannot be considered a special technical feature as defined in PCT Rule 13.2.

Further, according to PCT Rule 13.3, unity of invention should be evaluated without regard to whether the inventions are claimed as separate claims or as alternatives within a single claim.

Therefore, the inventions pertaining to polypeptides represented by SEQ ID Nos:1 to 20 and 25 set forth in the present claims cannot be considered as a group of inventions so linked as to form a single general inventive concept, but rather, are recognized as 21 invention groups pertaining to 21 different polypeptides.

Document 1: WO 03/016511 A1 (Takara Bio Inc.), 27 February 2003

4. Consequently, this opinion has been established in respect of the following parts of the international application:
   - ☒ all parts
   - ☐ the parts relating to claims Nos. _____

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Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims		YES
	Claims	1-24	NO
Inventive step (IS)	Claims		YES
	Claims	1-24	NO
Industrial applicability (IA)	Claims	1-24	YES
	Claims		NO

2. Citations and explanations:

Document 1: WO 03/016511 A1 (Takara Bio Inc.), 27 February 2003, & EP 1424387 A1

Document 2: *Proc. Natl. Acad. Sci. USA*, Vol. 80, No. 11, pages 3218-3222 (1983)

Claims 1 to 21

The inventions set forth in claims 1 to 21 lack novelty and do not involve an inventive step in the light of document 1 cited in the international search report.

Document 1 discloses the inducement of cytotoxic T lymphocytes using a culture including fibronectin and a fragment thereof (e.g. a VLA-4 binding domain, VLA-5 binding domain, or heparin binding domain). Further, document 1 lists C-274 (SEQ ID No.:1), H-271 (SEQ ID No.:3), H-296 (SEQ ID No.:4), CH-271 (SEQ ID No.:5), CH-296 (SEQ ID No.:6), C-CS1 (SEQ ID No.:7), CHV-89 (SEQ ID No.:8), CHV-90 (SEQ ID No.:9), CHV-92 (SEQ ID No.:10), CHV-179 (SEQ ID No.:11), CHV-181 (SEQ ID No.:12), and H-275-Cys (SEQ ID No.:13) as examples of said fragment.

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Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Claims 22 to 24

The inventions set forth in claims 22 to 24 lack novelty and do not involve an inventive step in the light of document 2 cited in the international search report.

Document 2 discloses cDNA encoding fibronectin which includes a sequence similar to the amino acid sequence described by SEQ ID No.:25 of the present application.

Said cDNA is recognized as being one which can be hybridized under stringent conditions with DNA comprising the base sequence described by SEQ ID No.:26, and used in the preparation of cytotoxic lymphocytes. Further, claims 22 and 24 stipulate the deletion, insertion, addition, or substitution of "a plurality of" amino acids (bases). Therefore, there is no limitation to the degree of genetic engineering, and thus, because it is obvious that the fibronectin disclosed in document 2 can be used in the preparation of cytotoxic lymphocytes, the inventions set forth in claims 22 to 24 and the invention disclosed in document 2 are indistinguishable.

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 10 and 12 specify "fibronectin fragments" in terms of SEQ ID Nos.:1 to 20 and 25. However, the only fragments which are confirmed in the description as having an effect relating to the preparation of cytotoxic lymphocytes are CH-296 (SEQ ID No.:13), H-296 (SEQ ID No.:11), and CH-296Na (SEQ ID No.:25). Therefore, the inventions set forth in claims 10 to 12 are not sufficiently supported by the description.